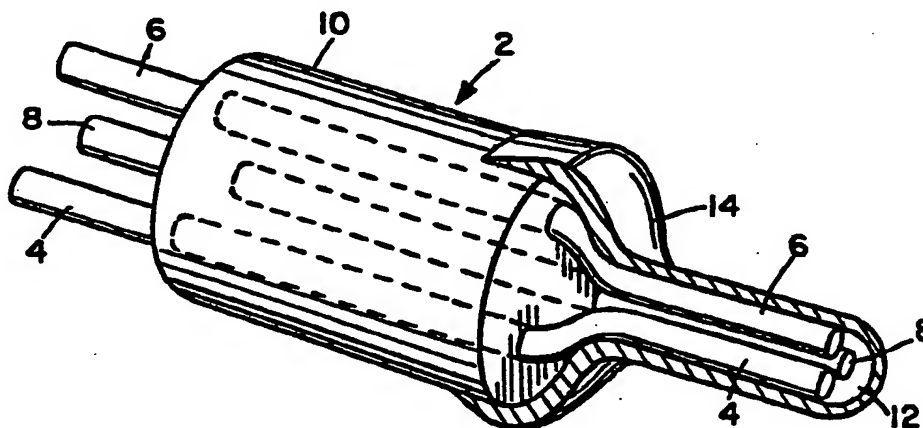




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : G01N 27/26	A1	(11) International Publication Number: WO 91/09302 (43) International Publication Date: 27 June 1991 (27.06.91)
<p>(21) International Application Number: PCT/US90/07345</p> <p>(22) International Filing Date: 13 December 1990 (13.12.90)</p> <p>(30) Priority data: 450,852 14 December 1989 (14.12.89) US</p> <p>(71) Applicant: THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 2199 Addison Street, Berkeley, CA 94720 (US).</p> <p>(72) Inventors: GOUGH, David, A. ; 1435 Big Canyon Terrace, Cardiff-By-The-Sea, CA 92007 (US). LUCISANO, Joseph, Y. ; 22871 West Tamarack Lane, Saugus, CA 91350 (US).</p>	<p>(74) Agents: MCCLAIN, James, W. et al.; Brown, Martin, Haller and McClain, 110 West "C" Street, Suite 1300, San Diego, CA 92101 (US).</p> <p>(81) Designated States: AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH (European patent), CM (OAPI patent), DE (European patent), DK (European patent), ES (European patent), FI, FR (European patent), GA (OAPI patent), GB (European patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU (European patent), MC, MG, ML (OAPI patent), MR (OAPI patent), MW, NL (European patent), NO, RO, SD, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent).</p> <p>Published <i>With international search report.</i></p>	

(54) Title: METHOD FOR INCREASING THE SERVICE LIFE OF AN IMPLANTABLE SENSOR



(57) Abstract

A method is described for extending the service life of implantable sensors having a corrodible reference electrode (4), at least one noble metal cathodic working electrode (6), and at least one noble metal anodic counter electrode (8) for the detection of oxygen and/or glucose in bodily fluids, which involves operating both the reference and the working electrodes with each in a first electrical state and prior to occurrence of sensor failure, changing the electrical state of at least one of the electrodes to a second electrical state and continuing operation in that second state beyond when the sensor would have failed had the first electrical state in both electrodes been maintained.

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1 METHOD FOR INCREASING THE SERVICE LIFE
2 OF AN IMPLANTABLE SENSOR

3 BACKGROUND OF THE INVENTION

4 FIELD OF THE INVENTION

5 The invention herein relates to implantable sensors for
6 measuring the concentrations of chemical species in bodily
7 fluids. More particularly it relates to methods of extending
8 the service life of such sensors.

9 DESCRIPTION OF THE PRIOR ART

10 The electrochemical oxygen sensor has been a powerful
11 tool for revealing the role of oxygen in biological systems.
12 Application of this sensor has been the main experimental
13 methodology in many thousands of studies over more than 40
14 years. Virtually all, however, have been studies in which the
15 sensor is used for a period of only a few days at most before
16 recalibration is necessary. More recently there has been
17 developed a stable oxygen sensor that is suitable for
18 continuous application in long-term monitoring situations
19 without the need of frequent recalibration. Such a sensor
20 makes possible certain important oxygen monitoring
21 applications that were not previously feasible.

22 This type of sensor, and its application as a component
23 of an enzyme electrode-based system for continuously

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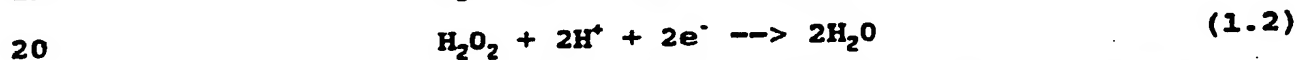
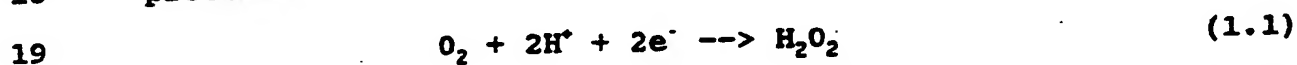
1 monitoring glucose, have been described in several prior
2 patents: U.S. Patents Nos. 4,650,547; 4,671,288; 4,703,756 and
3 4,781,798. The glucose monitoring system requires two oxygen
4 such sensors, one coupled to immobilized enzymes to detect
5 oxygen modulated by the enzyme reaction, and the other to
6 monitor the background oxygen concentration.

7 When a noble metal working electrode (usually platinum or
8 gold) is immersed in an electrically conductive medium and
9 held at a potential sufficiently cathodic with respect to an
10 appropriate reference electrode, oxygen molecules in contact
11 with the surface are reduced and an oxygen diffusion gradient
12 is established, resulting in an electrical current. The
13 current passes between the working and reference electrodes if
14 a two-electrode system is used, or mainly between the working
15 electrode and an indifferent counter electrode separate from
16 the reference electrode when a three-electrode system is used.
17 This phenomenon was observed and reported in the 19th century.
18 Under certain conditions, the reduction current may be related
19 to oxygen concentration in the medium. A membrane permeable
20 to oxygen can be placed over the electrodes to separate them
21 from the analyte medium and provide the appropriate conditions
22 for oxygen mass transfer and electrochemical oxygen reduction.
23 This principle forms the basis of amperometric (current-

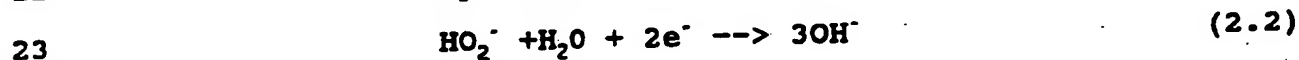
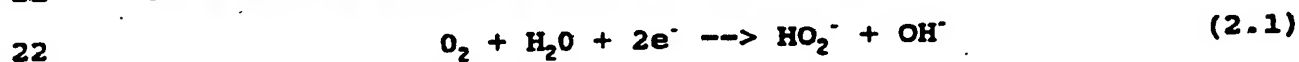
- 3 -

1 measuring) electrochemical oxygen sensors. Three electrode
2 amperometric sensors are often referred to as potentiometric
3 sensors, since they are operated by potentiostatic
4 instrumentation. It is recognized that the application of
5 this principle will be influenced by factors such as:
6 impurities in the media; Ph and reaction intermediates; oxygen
7 dissolved interstitially in the metallic electrode; the nature
8 of the background electrolyte; and the degree of electrode
9 surface oxide coverage.

10 The reaction pathways are complex. They include the
11 kinetics of oxygen adsorption on and into the electrode and
12 the formation of multiple metal-oxygen complexes involving
13 short-lived intermediates. A detailed consideration of these
14 pathways is not required here, but simplified models of the
15 electrode reactions that are believed to explain many aspects
16 are helpful in understanding the invention. One widely
17 accepted mechanism in acidic media is the following two-step
18 process:



21 In alkaline media, a similar process has been proposed:



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1 HO_2^- is the ionized form of H_2O_2 that is present in
2 alkaline media. These two sets of equations indicate that
3 oxygen reduction can proceed by either a 2 or 4 electron
4 process on platinum in aqueous solutions.

5 When the electrode is polarized within a certain cathodic
6 range, the rate of electrochemical reaction is sufficiently
7 rapid that the process becomes mass transfer limited and
8 determined by the mass transfer limitation of the membrane and
9 analyte medium. This results in a current "plateau," in which
10 there is relatively little variation in current with applied
11 potential. The electrode can be most easily operated as part
12 of a sensor in this potential range.

13 Certain three-electrode sensors of this type, especially
14 those described in the aforesaid U.S. Patents, have been shown
15 to have long-term stability under well-defined in vitro and in
16 vivo conditions. It has been found, however, that after a
17 period of operation, such sensors tend to fail in one or the
18 other of two characteristic modes. In most cases, the current
19 rose abruptly and returned to the original value several times
20 over the period of a few hours before finally remaining at a
21 high, off-scale value. In other sensors, the current suddenly
22 began to drift downward and fell over a period of several
23 weeks.

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1 It would be of significant value to have a method for
2 preventing or deferring such failures, since such would be
3 expected to substantially increase the operating service life
4 of the sensors. It is therefore an object of this invention
5 to provide such a method.
6

7 SUMMARY OF THE INVENTION

8 The invention herein is a method for extending the
9 service life of implantable sensors containing potentially
10 corrodible electrodes (preferably such as silver or silver-
11 impregnated electrodes), particularly sensors for the
12 detection of oxygen and/or glucose in bodily fluids.
13 Specifically, the invention is a method comprising, in a
14 sensor having a potentially corrodible reference electrode, at
15 least one noble metal cathodic working electrode, and at least
16 one noble metal anodic counter electrode maintained at a low
17 impedance, operating both the reference electrode and the
18 working electrode in the sensor with each in a first
19 electrical state, and prior to occurrence of sensor failure,
20 changing the electrical state of at least one of the reference
21 electrode and the working electrode to a second electrical
22 state and continuing operation of the sensor in that second
23 state for a period of time extending beyond the time at which

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1 the sensor would have failed had the first electrical state in
2 both electrodes been maintained.

3 In specific embodiments, the change in the electrical
4 state of one or both of the working and reference electrodes
5 may comprise: increasing the impedance at the reference
6 electrode, preferably while shielding the electrode against
7 effects of stray capacitance; electrically reversing the two
8 electrodes; having a plurality of working and/or reference
9 electrodes present, with only one of each active at any time,
10 and sequentially replacing the operating electrode in the
11 sensor circuitry with a second like electrode which was
12 previously inactive; periodically reversing the electrical
13 potential to the working and the reference electrodes and
14 maintaining that reversed state for an extended time; and/or
15 causing a small, continuous cathodic current to pass through
16 the reference electrode.

17

18

BRIEF DESCRIPTION OF THE DRAWINGS

19

20

21

FIGURE 1 is a perspective view, partially cut away,
illustrating the basic sensor design applicable to this
invention.

22

23

FIGURE 2 is an schematic electrical diagram showing the
basic circuitry of the sensors applicable to this invention.

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1 FIGURE 3 is an schematic electrical diagram showing the
2 circuitry of an embodiment of this invention in which a
3 plurality of working and/or reference electrodes is used.

4 FIGURE 4 is an schematic electrical diagram showing the
5 circuitry of an embodiment of this invention in which the
6 polarities of the working and reference electrodes are
7 reversible.

8 FIGURE 5 is an schematic electrical diagram showing the
9 circuitry of an embodiment of this invention in which the
10 functions of the working and counter electrodes are
11 reversible.

12 FIGURE 6 is a schematic electrical diagram showing the
13 circuitry of an embodiment of this invention in which a small
14 cathodic current is caused to pass through the reference
15 electrode.

16 17 DETAILED DESCRIPTION OF THE INVENTION

18 This invention is the result of discoveries made during
19 the study of the failure mechanisms of the sensors described
20 in the above-cited patents. It is therefore important to
21 describe the normal operation of such sensors and the
22 discoveries made about the failure modes, so that the method
23 of this invention and its specific embodiments for extending

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1 the service life of such sensors will be fully understood.

2 The basic sensor is illustrated in Figure 1. The
3 platinum working electrode 6, the silver/silver chloride
4 reference electrode 4 and the platinum counter electrode 8 are
5 fine wires embedded in an epoxy resin or glass cylinder 10 and
6 connected to more substantial lead wires not shown. The active
7 electrodes extend from one end of the insulating cylinder and
8 the lead wires extend from the opposite end. The electrodes
9 are in electrolytic contact through an aqueous electrolyte gel
10 12 and encased by an outer hydrophobic layer 16. The thin,
11 cylindrical shape of the active region of this oxygen sensor
12 readily allows for its inclusion in the two-dimensional
13 glucose sensor described in the above-cited patents.
14 Alternatively, one or more of the electrodes may take the form
15 of disks instead of cylinders, with the exposed surface flush
16 with the surface of the insulating cylinder.

17 Test sensors were disassembled after a period of
18 operation (commonly 120 days) for detailed microscopic
19 examination. In a typical analysis, it was found that the
20 reference electrode (originally formed from a solid silver
21 wire, of constant 0.075 mm diameter) had partially dissolved,
22 had become porous and had significantly corroded, with only
23 approximately one half of its original material remaining at

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1 the time of examination. The degree of corrosion observed was
2 approximately proportional to the time of operation of the
3 sensor. Similar examinations of the working electrode showed
4 that it had acquired a granular surface structure with use,
5 which, according to X-ray elemental analysis, was a deposition
6 of a thin layer of silver.

7 In the cases of gradual sensor failure, the original
8 signal could be restored by appropriate polarization treatment
9 of the working electrode. In cases of abrupt sensor failure,
10 a dendritic silver structure had formed a contact between the
11 working and reference electrodes, apparently growing from the
12 working electrode. In all cases, the counter electrode
13 retained its original surface composition and microstructure
14 and otherwise showed no change.

15 The microscopic examination indicates that various
16 processes are believed to occur during operation. The working
17 electrode gradually becomes coated with silver as a result of
18 being cathodically polarized with respect to the silver
19 source, the reference electrode. At that point, the
20 oxygen-reduction process no longer occurs on the underlying
21 platinum surfaces but continues unaffected on the deposited
22 outer silver coating. The deposition of silver apparently
23 does not affect the signal as long as no dendritic contact

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1 with the other electrodes is made. The transfer of silver
2 from the reference electrode was, however, somewhat surprising
3 because the reference electrode is maintained at very high
4 impedance by the potentiostat circuit ($>10^{12} \Omega$ based on the
5 input impedance of the reference operational amplifier).
6 Calculations show that a leakage current of 10^{-12} A between the
7 two electrodes is sufficient in some cases to account for the
8 small amount of material transferred. Transient local
9 capacitive currents as a result of inadequate shielding of the
10 lead wires may also have played a role. These currents,
11 induced by external electromagnetic fields, were observed to
12 reach peak values as high as 5×10^{-9} A in other experiments
13 involving electrodes placed in electrically "noisy"
14 environments.

15 In most cases, sensor lifetime was limited by corrosion
16 of the reference electrode, with failure occurring when a
17 dendritic contact (a deposit formed from dissolved silver)
18 ultimately connected the working and reference electrodes.

19 Based on these observations, the various embodiments of
20 the method of this invention were developed. All rely on the
21 basic principle of changing at least one of the working
22 electrode and the reference electrode from the electrical
23 state in which it is originally operated to a second

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1 electrical state, and then continuing the operation of the
2 sensor with the electrode or electrodes operating in that
3 second electrical state. It is believed that the prolongation
4 of the service life of the sensors operated according to the
5 method of this invention is due to the change in electrical
6 state reversing or slowing the transfer of metal from one
7 electrode to the other and/or the formation of dendritic
8 structures of metal between the electrodes.

9 One embodiment of the present method comprises increasing
10 the input impedance at the reference electrode, preferably
11 while shielding the electrode to counteract the effects of
12 stray capacitance which would cause local currents. It is
13 recognized, however, that since the initial impedance is
14 already high ($>10^{12} \Omega$) this embodiment, while showing a
15 definite effect, is somewhat limited in its long-term
16 potential and is therefore less preferred than other
17 embodiments described.

18 A second embodiment comprises, prior to formation of any
19 dendritic structure bridging the two electrodes, reversing the
20 electrical connections to the working and counter electrodes,
21 as shown in Figure 3, so that each assumes the prior operating
22 role of the other. This will cause the new counter electrode
23 to become cleaned of its accumulated layer of deposited silver

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1 and silver to become deposited on the new working electrode.
2 This reversal can be repeated as long as the reference
3 electrode remains functional and contains a sufficient amount
4 of silver. This would require a relatively large reference
5 electrode.

6 A third embodiment comprises including in the sensor
7 structure a plurality of working and/or reference electrodes,
8 as shown in Figure 4. Only one of each type of electrode
9 would be operative as a working or reference electrode at any
10 one time, and all electrodes of each type would be designed so
11 that they could be connected sequentially into the sensor
12 circuit. Thus as each working and/or reference electrode
13 approached the limit of its service life because of metal
14 deposition or removal, a second previously unused electrode
15 could be switched into its place. In a preferred version of
16 this embodiment, the extra working electrodes are initially
17 incorporated into the sensor circuitry as counter electrodes
18 and each operates as such until such time as it is needed as
19 a replacement working electrode. This will enable the reserve
20 working electrodes to maintain a deposit-free surface until
21 each is used as a replacement for a previous working
22 electrode.

23 With respect to the reserve reference electrodes, these

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1 would be most effective if they were relatively large.

2 The fourth embodiment of this present method comprises
3 periodically reversing the electrodes' polarization so as to
4 drive electrodeposited metal (usually silver) from working
5 electrode back to the reference electrode. This can be
6 accomplished by reversing the polarity of the circuit such
7 that the silver reference electrode becomes cathodic and the
8 working electrode becomes anodic for a period of time
9 sufficient to pass the required number of coulombs of silver
10 from the working electrode to the reference electrode.

11 The fifth embodiment of this present method comprises
12 employing means to pass a small, continuous cathodic current
13 through the reference electrode. This current, while not
14 large enough to cause significant polarization of the
15 electrode, functions to prevent corrosion of the electrode
16 material.

17 It will be recognized that these embodiments may be used
18 in various combinations with each other, and that such
19 combinations may produce further extended service lifetimes.
20 For example, a plurality of working and/or reference
21 electrodes may be present and may be switched into the system,
22 while at the same time the service life of each individual
23 electrode may be extended by reversing the electrode's

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1 polarization periodically. This should result in a extension
2 of the service life of each individual electrode and thus
3 extend the time between the necessary replacements of
4 electrodes from the plural supply of electrodes. Also, any
5 reference electrode currently in use may be impressed with a
6 small cathodic current to reduce its rate of corrosion. Thus
7 the cumulative effect of the combination of embodiments is a
8 greatly extended service life for the sensor itself, and much
9 longer intervals between implantations of fresh sensors.

10 Examination of the Figures of the drawings will further
11 explain the embodiments of this invention. Referring first to
12 Figure 1, the basic sensor 2 used in the present method is
13 illustrated. There are three electrodes, the reference
14 electrode 4, the working electrode 6 and the counter electrode
15 8. The reference electrode 4 is a silver/silver chloride
16 electrode while the working electrode 6 and counter electrode
17 8 are noble metal (preferably platinum) electrodes. The three
18 electrodes are formed of fine wire embedded in a glass or
19 epoxy cylindrical housing 10 and are connected to more
20 substantial lead wires (not shown). The electrodes are in
21 electrical contact through an aqueous electrolyte gel 12. The
22 electrodes 4, 6 and 8 are clustered outside of the housing 10
23 in a narrowed or necked region 14 which is covered by a

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1 hydrophobic oxygen permeable layer 16 of a material such as
2 silicone rubber.

3 The sensor 2 is operated on the classical potentiostatic
4 principle which is illustrated schematically in Figure 2. As
5 with other types of sensors, oxygen is electrochemically
6 reduced at the surface of the platinum working electrode 6,
7 generating an electrode current that is proportional to the
8 oxygen flux. The potential of the platinum working electrode
9 is specified with respect to the silver/silver chloride
10 reference electrode 4. In this mode of operation however, the
11 reference electrode 4 is maintained electronically at a very
12 high impedance to avoid significant current uptake. The main
13 current passes to the inert counter electrode 8, which is
14 maintained at low impedance. The operational amplifier
15 circuitry 18 maintains the desired potential between the
16 working and reference electrodes 6 and 4 by applying the
17 appropriate potential between the working and counter
18 electrodes 6 and 8. The voltage developed across the feedback
19 resistor R_f is proportional to the electrode current. This
20 voltage is measured and processed by other circuitry not
21 shown.

22 This three-electrode system provides separate electrodes
23 for the two functions carried out by the anode in previous

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1 designs and has the advantage of directing very little current
2 to the reference electrode 4. It makes possible the use of
3 much larger ratios of the area of working electrode 6 to that
4 of counter electrode 8, thereby producing larger currents.
5 This makes signal amplification and noise reduction less
6 critical in sensors of small overall size.

7 Embodiments of the method are illustrated graphically in
8 Figures 3-6. Figure 3 shows an embodiment in which there are
9 a plurality of working electrodes which can be switched
10 sequentially into the system. Three electrodes (labeled A, B
11 and C) comprise the working and reference electrodes. In the
12 version shown in Figure 3, electrode A is wired as the working
13 electrode, electrode B is wired as an extra counter electrode
14 (along with regular counter electrode 8) and electrode C is
15 out of the circuitry. The selection of which electrode is the
16 working electrode at any given time is by means of the
17 combination of 3-pole, sequential throw switch 20 and the
18 individual SPDT-center off switches 22 (respectively 22A, 22B
19 and 22C in each path). As each working electrode becomes
20 deteriorated or subject to coating or bridging, it is switched
21 out of the circuit by opening its switch 22 (i.e., moving the
22 switch to the center-off position as at 22C), moving the
23 switch 20 to the next sequential position and closing that

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1 next electrode's switch 22 as shown at 22A. While the
2 remaining fresh electrodes can be left out of the system (by
3 having their switches 22 left open) if desired, it is
4 preferred to have them temporarily wired into the circuit as
5 additional counter electrodes as shown with electrode B and
6 switch 22B to prevent them from becoming coated with metal
7 deposits.

8 It will be apparent that Figure 3 also illustrates the
9 type of circuitry necessary for having a plurality of
10 switchable reference electrodes. In this case the switch 20
11 would be placed in line 24 between the battery 26 and the
12 plurality of electrodes. Each of the switches 22 could be
13 SPST switches which would all be open except for the
14 particular electrode which was then in use, since there is no
15 purpose in having the extra electrodes alternatively serve as
16 counter electrodes. One can also combine the presence of both
17 extra working and reference electrodes by having separate
18 switches 20 in each line 24 and 28 and sequencing the two
19 parts of the circuit independently as needed.

20 While only three electrodes are shown in Figure 3, it
21 will be evident that there can be any number, limited only by
22 the number of electrode wires which can conveniently be
23 clustered in the sensor 2 in combination with the electrodes

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1 4, 6 and 8.

2 Figure 4 illustrates the embodiment where the polarity of
3 the working and reference electrodes are reversible. In this
4 case lines 24 and 28 lead into DPDT switch 34 which is wired
5 such that throwing the switch reverses the leads to electrodes
6 30 and 32. Thus the electrodes 30 and 32 are connected
7 alternatively as the working electrode in line 28 or the
8 reference electrode in line 24.

9 Figure 5 illustrates the embodiment where the functions
10 of the working and counter electrodes are reversible. In this
11 case lines 28 and 42 (the latter from ground 48) lead into
12 DPDT switch 36 which is wired such that throwing the switch
13 reverses the connections between lines 28 and 42 and the leads
14 38 and 40 from electrodes 44 and 46. Thus the electrodes 44
15 and 46 are connected alternatively as the working electrode in
16 line 28 or the counter electrode grounded through line 42.

17 Figure 6 illustrates the embodiment where a controlled
18 current source 50 is placed between the working electrode lead
19 52 and the reference electrode lead 54. This current source
20 functions to pass a small, continuous cathodic current through
21 the reference electrode 6. It will be recognized that the
22 current source could be also placed in other areas of the
23 circuit and achieve the same result.

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1 The following examples will illustrate the sensors to
2 which the service life extension method and embodiments of
3 this invention can be applied. Electrodes were made by
4 welding a small segment of 0.003 or 0.005-in.-diameter
5 platinum or silver wire to one end of a long, PTFE-insulated
6 stainless steel lead wire. The welded regions of two such
7 platinum electrodes and one silver electrode were then
8 encapsulated individually in the lumens of a short segment of
9 multibore borosilicate glass tubing (0.010-in.-i.d.,
10 0.062-in.-o.d.; Friedrich and Dimmock, Inc.) so that the
11 electrodes and lead wires extended from opposite ends of the
12 glass housing. A bisphenol A/epichlorohydrin-based epoxy resin
13 (Stycast 1266, Emerson and Cuming, Inc.) was used for the
14 encapsulation. Electrodes were carefully bent to the parallel
15 arrangement shown in Figure 1 and trimmed to a length of
16 0.02-0.10 in. The working and counter electrodes were
17 platinized to a roughness factor of approximately 800, as
18 estimated by anodic hydrogen stripping. The electrolyte gel
19 was formed around the electrodes by dipping the end of the
20 assembly in a 10-20% solution of poly(hydroxyethyl
21 methacrylate) (Polysciences, Inc.) in methanol, allowing the
22 solvent to evaporate, and hydrating with electrolyte. The
23 electrolyte was 0.01 M phosphate buffer, pH 7.3, containing

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1 0.01 M KCl. The gel filled in the spaces between the
2 electrodes and provided a thin coating on the outer aspects.
3 After drying, the outer hydrophobic layer was formed by
4 dipping the end of the assembly in a solution of 25% silicone
5 rubber (RTV 3140, Dow Corning Corp.) in toluene. The solvent
6 was evaporated and the silicone rubber allowed to cure. This
7 produced a layer approximately 10-25 μ m thick. The gel could
8 be dehydrated and rehydrated by exposure to an aqueous sample
9 without loss of activity. The assembly was then fixed in a
10 silicone rubber tube (0.040-in.-i.d., 0.085-in.-o.d., Dow
11 Corning Corp.) in such a way that the lead wires were extended
12 inside the tube and the active electrode region occupied one
13 end. This recessed design presents an annular space around the
14 electrodes which may be filled with an enzyme gel for enzyme
15 electrode applications. The annular cavity was filled with
16 silicone rubber (RTV 3140) or the tube was trimmed to expose
17 the hydrophobic membrane-covered electrode assembly. The space
18 surrounding the lead wires was filled with silicone rubber
19 (RTV 615, General Electric Co.) to provide mechanical
20 strength. A miniature electrical connector (Microtech, Inc.)
21 was attached to the lead wires at their exit from the tube.
22 This simple fabrication approach typically gave a high yield
23 of sturdy, functional sensors.

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1 Sensors were checked for uniformity prior to long-term
2 testing. The integrity of the silicone rubber coating was
3 determined by measuring the resistance with respect to an
4 external electrode using a high impedance electrometer
5 (Keithley Instruments Co., Model 616). Sensors with an
6 apparent resistance of $10 \times 10^9 \Omega$ or greater could be used in
7 complex media without interference from diffusible polar
8 solutes and were considered to have an effective barrier.
9 Sensors with significantly lower apparent resistance were
10 recoated. The background current in the absence of oxygen was
11 measured and determined to be insignificant. Linearity of the
12 response over a physiologic oxygen concentration range was
13 verified by exposing sensors to oxygen concentrations ranging
14 from 0.02 to 0.24 mM, made by equilibrating buffer solutions
15 with analyzed gas mixtures of 2, 5, 10 and 21% oxygen. Sensors
16 typically required approximately one minute to return to
17 steady-state after a step change in oxygen concentration.

18 Sensors were evaluated for stability in sealed,
19 thermostated vessels at 37°C, containing 0.01 M phosphate
20 buffer, pH 7.3. Solutions were maintained at desired oxygen
21 concentrations by equilibration with analyzed gas mixtures.
22 The concentration was changed at intervals of several days to
23 demonstrate sensitivity. Electrode current was recorded

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1 continuously.

2 Six sensors were operated continuously in a sealed,
3 thermostated vessel at 37°C, containing 0.01 M phosphate
4 buffer, pH 7.3. The oxygen concentration was maintained at
5 atmospheric levels by equilibration with filtered room air.
6 Some sensors incorporated specific design modifications
7 described below to determine their influence on reference
8 electrode degradation. Sensors were otherwise identical to
9 that shown in Figure 1. Five sensors were disassembled after
10 70 days of continuous operation. One sensor was disassembled
11 after 10 days of continuous operation. Reference electrodes
12 were removed from the sensors and scanning electron microscopy
13 was used to assess the extent of reference electrode
14 degradation in each case. All reference electrodes were
15 originally formed from solid, 0.075-mm-diameter silver wire.

16 A reference electrode was taken from a sensor that was
17 subjected to the test conditions for 70 days but was not
18 connected to any external circuitry to provide polarization of
19 the working electrode. In this case, all electrodes were
20 maintained at "open circuit" and were therefore not capable of
21 sustaining DC current. This electrode served as a control in
22 the experiment, since any corrosion in this case would be the
23 result of simple electrolyte-silver interaction or passive

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1 noise pickup in the lead wires. Inspection by micrograph
2 revealed little or no corrosion of this electrode.

3 Analysis by micrographs was made of reference electrodes
4 taken from sensors that employed unshielded and shielded
5 reference electrode lead wires, respectively. Both of these
6 sensors were operated continuously for 70 days prior to
7 disassembly. The reference electrode from the unshielded
8 sensor exhibited substantially more corrosion than that from
9 the shielded sensor. However, even the electrode in the
10 shielded case showed significant corrosion over 20-30% of its
11 surface. This indicates that lead wire shielding, although
12 helpful in reducing corrosion, does not eliminate it totally
13 under the conditions described here.

14 Also analyzed by micrograph was a reference electrode
15 taken from a sensor that lacked an outer hydrophobic membrane.
16 This sensor was operated continuously for 70 days prior to
17 disassembly. The electrode showed only minimal corrosion. The
18 absence of the hydrophobic membrane in this case allows
19 products from the anode and cathode reactions to diffuse out
20 of the electrolyte gel surrounding the electrodes. This
21 results in a lower steady-state concentration of those species
22 at the surface of the reference electrode during sensor
23 operation. The minimal degradation of this reference electrode

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1 suggests that the unidentified reaction products may be
2 inherently corrosive to the electrode. Alternatively, the
3 altered distribution of ionic current between the working and
4 counter electrodes could be responsible for the decreased
5 corrosion in this case.

6 Also analyzed by micrographs were reference electrodes
7 taken from sensors operated continuously for 10 and 70 days
8 respectively prior to disassembly. In these two cases,
9 reference electrodes were subjected to a constant d.c. current
10 instead of being maintained at high impedance. The current
11 density in each case was 5.0×10^{-7} A/cm². One reference
12 electrode was subjected to an anodic current, while the other
13 electrode was subjected to a cathodic current. The
14 polarization induced in these electrodes by the forced current
15 was measured and found to be less than 0.5 mV. These results
16 dramatically demonstrate the effects of DC leakage currents on
17 reference electrode corrosion. The sensor with impressed
18 anodic current operated for only 10 days before failing due to
19 dendritic contact between the reference and working
20 electrodes. The corrosion rate of the reference electrode in
21 this sensor was much greater than that of any other
22 configuration. The sensor with impressed cathodic current,
23 however, demonstrated a very low corrosion rate, as indicated

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1 by the lack of surface pitting. Some surface deposits
2 (probably silver chloride) were noticeable on this specimen.

3 It will be evident that there are other embodiments that
4 are not expressly set forth above but which are clearly within
5 the scope and spirit of the invention. Therefore the above
6 description is to be considered exemplary only and the scope
7 of the invention is to be defined solely by the appended
8 claims.

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CLAIMS

1. A method for extending the service life of implantable
2 sensors containing corrodible electrodes, which comprises, in
a sensor having a corrodible reference electrode, at least one
4 noble metal cathodic working electrode, and at least one noble
metal anodic counter electrode maintained at a low impedance,
6 operating both said reference electrode and said working
electrode in said sensor with each in a first electrical
8 state, and prior to occurrence of sensor failure, changing
the electrical state of at least one of said reference
10 electrode and said working electrode to a second electrical
state and continuing operation of said sensor in said second
12 state for a period of time extending beyond the time at which
said sensor would have failed had said first electrical state
14 in both electrodes been maintained.

2. A method as in Claim 1 wherein said corrodible electrode
2 is a silver or silver-impregnated electrode.

3. A method as in Claim 1 wherein said changing of said
2 electrical state comprises increasing the input impedance at
the reference electrode.

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2 4. A method as in Claim 3 wherein said reference electrode is also shielded to counteract the effects of stray capacitance which would cause local currents.

2 5. A method as in Claim 1 wherein said changing of said electrical state comprises, prior to formation of any dendritic structure bridging the said working and reference
4 electrodes, reversing the electrical connections to said working and counter electrodes so that each assumes the prior
6 operating role of the other.

2 6. A method as in Claim 1 wherein changing said electrical state comprises including in said sensor a plurality of working or reference electrodes, with only one of said
4 plurality of electrodes operative at any one time, with all of said electrodes adapted to be connected sequentially into the
6 sensor circuit.

2 7. A method as in Claim 6 wherein there are pluralities of both said working and said reference electrodes, and in each
4 plurality said electrodes are adapted to be connected sequentially into said circuit.

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8. A method as in Claim 6 wherein said plurality is of said
2 working electrodes and those electrodes in said plurality
which have not yet been used as the operative working
4 electrode are connected in said circuit as additional counter
electrodes and each operates as such until such time as it is
6 switched into said circuit as a replacement working electrode.

9. A method as in Claim 8 wherein, in said plurality of said
2 working electrodes, electrodes in said plurality which have
not yet been used as the operative working electrode are
4 connected in said circuit as additional counter electrodes and
each operates as such until such time as it is switched into
6 said circuit as a replacement working electrode.

10. A method as in Claim 1 wherein said changing of said
2 electrical state comprises periodically changing the
polarization of said working and reference electrodes so as to
4 drive electrodeposited metal from working electrode back to
the reference electrode.

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11. A method as in Claim 10 wherein said changing of said
2 polarization comprises reversing the polarity of said circuit
such that said reference electrode becomes cathodic and said
4 working electrode becomes anodic for a period of time
sufficient to pass the required number of coulombs of silver
6 from said working electrode to said reference electrode.

12. A method as in Claim 1 wherein said changing of said
2 electrical state comprises applying to said reference
electrode a small, continuous, cathodic current.

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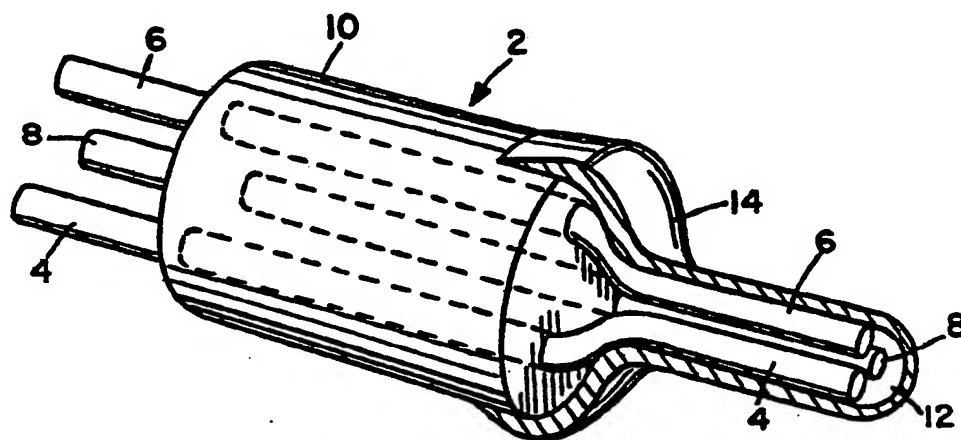


FIG. 1

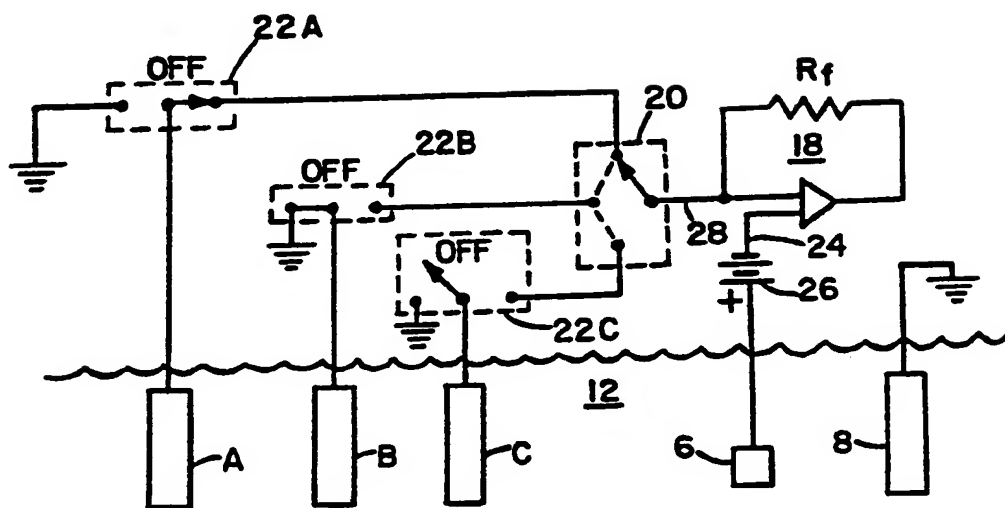


FIG. 3

2/2

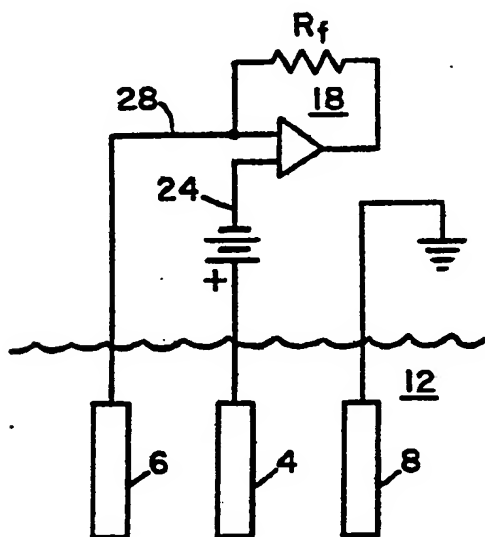


FIG. 2

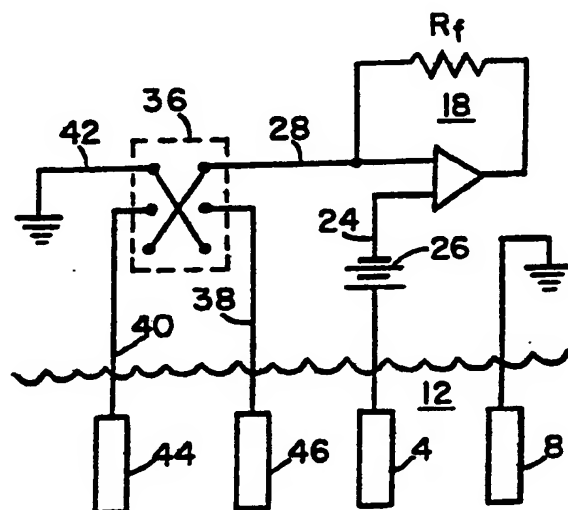


FIG. 5

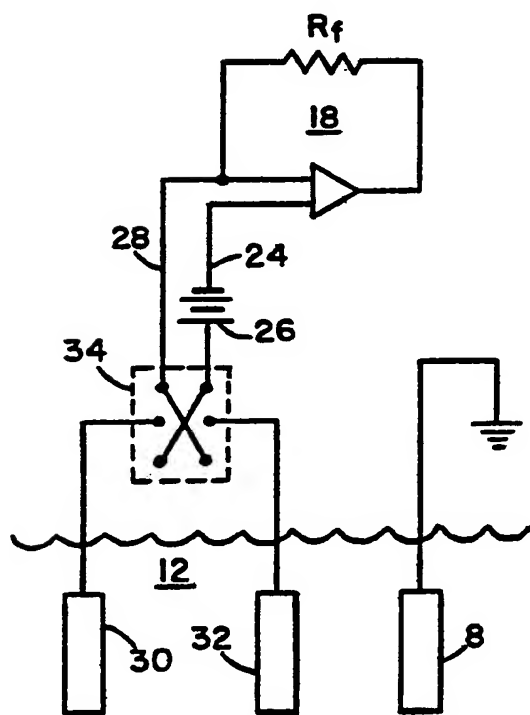


FIG. 4

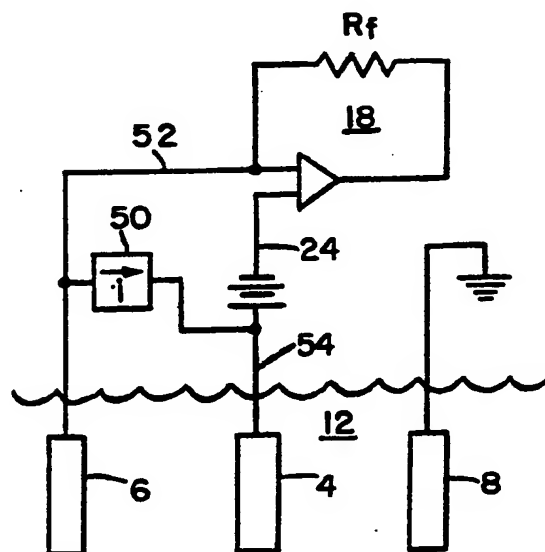


FIG. 6

INTERNATIONAL SEARCH REPORT

International Application No. **PCT/US90/07345**

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) * According to International Patent Classification (IPC) or to both National Classification and IPC <div style="display: flex; justify-content: space-between;"> INT. CL. (5) G01N 27/26 U.S. CL. 204/153.1 </div>																													
II. FIELDS SEARCHED <div style="display: flex; justify-content: space-between;"> <div style="width: 25%;"> Classification System <div style="border: 1px solid black; padding: 5px; margin-top: 5px;">U.S.</div> </div> <div style="width: 75%;"> Minimum Documentation Searched 7 Classification Symbols <div style="border: 1px solid black; padding: 5px; margin-top: 5px;">204/153.1, 153.2, 153.17, 400, 402, 403, 412, 415</div> </div> </div> <div style="margin-top: 10px;"> Documentation Searched other than Minimum Documentation to the extent that such Documents are included in the Fields Searched * </div>																													
III. DOCUMENTS CONSIDERED TO BE RELEVANT * <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%;">Category *</th> <th style="width: 70%;">Citation of Document, 11 with indication, where appropriate, of the relevant passages 12</th> <th style="width: 20%;">Relevant to Claim No. 13</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">Y</td> <td>US, A, 2,508,523, (Krebs), 23 May 1950 See column 4, lines 54-62</td> <td style="text-align: center;">12</td> </tr> <tr> <td style="text-align: center;">Y</td> <td>US, A, 2,563,062 (Perley), 07 August 1951 See figures 1-3</td> <td style="text-align: center;">4</td> </tr> <tr> <td style="text-align: center;">Y</td> <td>US, A, 2,805,191 (Hersch), 03 September 1957 See column 4, lines 66-75</td> <td style="text-align: center;">5,10,11</td> </tr> <tr> <td style="text-align: center;">Y</td> <td>US, A, 2,864,750 (Hughes et al), 16 December 1958 See column 4</td> <td style="text-align: center;">5,10,11</td> </tr> <tr> <td style="text-align: center;">Y</td> <td>US, A, 2,998,371 (Sabins), 29 August 1961 See columns 7, 8 and 12</td> <td style="text-align: center;">5-11</td> </tr> <tr> <td style="text-align: center;">A</td> <td>US, A, 3,246,235 (Allsopp), 12 April 1966 See figure 3</td> <td style="text-align: center;">1-12</td> </tr> <tr> <td style="text-align: center;">A</td> <td>US, A, 3,249,520 (Hermann), 03 May 1966, See figures 1-6</td> <td style="text-align: center;">1-12</td> </tr> <tr> <td style="text-align: center;">A</td> <td>US, A, 3,308,046 (Suleski), 07 March 1967 See figure 1b</td> <td style="text-align: center;">1-12</td> </tr> </tbody> </table>			Category *	Citation of Document, 11 with indication, where appropriate, of the relevant passages 12	Relevant to Claim No. 13	Y	US, A, 2,508,523, (Krebs), 23 May 1950 See column 4, lines 54-62	12	Y	US, A, 2,563,062 (Perley), 07 August 1951 See figures 1-3	4	Y	US, A, 2,805,191 (Hersch), 03 September 1957 See column 4, lines 66-75	5,10,11	Y	US, A, 2,864,750 (Hughes et al), 16 December 1958 See column 4	5,10,11	Y	US, A, 2,998,371 (Sabins), 29 August 1961 See columns 7, 8 and 12	5-11	A	US, A, 3,246,235 (Allsopp), 12 April 1966 See figure 3	1-12	A	US, A, 3,249,520 (Hermann), 03 May 1966, See figures 1-6	1-12	A	US, A, 3,308,046 (Suleski), 07 March 1967 See figure 1b	1-12
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<div style="display: flex;"> <div style="width: 50%;"> <p>* Special categories of cited documents: 10</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 50%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"A" document member of the same patent family</p> </div> </div>																													
IV. CERTIFICATION <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; vertical-align: top;"> Date of the Actual Completion of the International Search <div style="border: 1px solid black; padding: 5px; margin-top: 5px;">27 February 1991</div> </td> <td style="width: 50%; vertical-align: top;"> Date of Mailing of this International Search Report <div style="border: 1px solid black; padding: 5px; margin-top: 5px; font-size: 1.2em; font-weight: bold;">05 APR 1991</div> </td> </tr> <tr> <td style="vertical-align: top;"> International Searching Authority <div style="border: 1px solid black; padding: 5px; margin-top: 5px;">ISA/US</div> </td> <td style="vertical-align: top;"> Signature of Authorized Officer <i>Nguyen</i> <div style="display: flex; justify-content: space-between; margin-top: 5px;"> NGUYEN NGOC-HO INTERNATIONAL DIVISION </div> </td> </tr> </table>			Date of the Actual Completion of the International Search <div style="border: 1px solid black; padding: 5px; margin-top: 5px;">27 February 1991</div>	Date of Mailing of this International Search Report <div style="border: 1px solid black; padding: 5px; margin-top: 5px; font-size: 1.2em; font-weight: bold;">05 APR 1991</div>	International Searching Authority <div style="border: 1px solid black; padding: 5px; margin-top: 5px;">ISA/US</div>	Signature of Authorized Officer <i>Nguyen</i> <div style="display: flex; justify-content: space-between; margin-top: 5px;"> NGUYEN NGOC-HO INTERNATIONAL DIVISION </div>																							
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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US, A, 3,300,345 (Lyons), 24 January 1967 See figures 1-4	1-12
Y	US, A, 3,458,421 (Dahams), 29 July 1969 See column 4, line 11	5,10,11
A	US, A, 3,616,412 (Gnage), 26 October 1971 See the abstract	1-12
A	US, A, 4,036,716, (Hulthe), 19 July 1977, See the abstract	1-12
A	US, A, 4,088,550 (Malkin), 09 May 1978 See the abstract	1-12
A	US, A, 4,306,952 (Jansen), 22 December 1981 See the abstract	1-12
A	US, A, 4,650,547 (Gough), 17 March 1987 See columns 5 and 6	1-12
A	US, A, 4,671,288 (Gough), 09 June 1987 See figures 6 and 7	1-12
A	US, A, 4,703,756 (Gough et al.), 03 November 1987 See figure 2	1-12
A	US, A, 4,781,798 (Gough), 01 November 1988 See the abstract	1-12
A	US, A, 4,830,713 (Gagescu), 16 May 1989 See the abstract	1-12
Y	Joseph Y. Lucisano et al., "In Vitro Stability of an Oxygen Sensor", Reprinted from <u>Analytical Chemistry</u> , Volume 59, (1987), pp. 736-739	1-12
X Y	Joseph Y. Lucipano, "Development of an Implantable Glucose Sensor: Stability of the Oxygen Electrode and Analysis of the Transient Response", dissertation, Univ. of Calif. (San Diego), pp. 8-10, 26-30, 34-36, 96 and 97. (Dec. 15, 1988). See pages 34-36 and 43.	1-4,12 5-11

